

## Supporting Information

# A New Mass Spectrometry Based Approach for Organic Synthesis Monitoring

Veronica Termopoli<sup>1‡</sup>, Elena Torrisi<sup>4</sup>, Giorgio Famiglini<sup>1</sup>, Pierangela Palma<sup>1,2</sup>, Giovanni Zappia<sup>4</sup>,  
Achille Cappiello<sup>1,2\*</sup>

and

Gregory W. Vandergrift<sup>2,3‡</sup>, Misha Zvekic<sup>2</sup>, Erik T. Krogh<sup>2,3</sup>, Chris G. Gill<sup>2,3,5,6\*</sup>

<sup>1</sup> LC-MS Laboratory, Department of Pure and Applied Sciences, University of Urbino Carlo Bo, Urbino, Italy, 61029

<sup>2</sup> Applied Environmental Research Laboratories (AERL), Chemistry Department, Vancouver Island University, Nanaimo, BC, Canada, V9R 5S5

<sup>3</sup> Chemistry Department, University of Victoria, Victoria, BC, Canada, V8P 5C2

<sup>4</sup> Biomolecular Sciences Department, University of Urbino Carlo Bo, Urbino, Italy, 61029

<sup>5</sup> Chemistry Department, Simon Fraser University, Burnaby, BC, Canada, V5A 1S6

<sup>6</sup> Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, WA, USA, 98195

## Corresponding Authors

\* Professor Chris G. Gill, Ph.D., P. Chem.

Co-Director, Applied Environmental Research Laboratories (AERL) Chemistry Department  
Vancouver Island University

900 Fifth Street, Nanaimo, BC

Canada V9R 5S5

Ph: 250-753-3245

[Chris.Gill@viu.ca](mailto:Chris.Gill@viu.ca)

\* Professor Achille Cappiello

LC-MS Laboratory, Department of Pure and Applied Sciences

University of Urbino

Piazza Rinascimento, 6

Urbino, Italy

Ph: +390722303344

[achille.cappiello@uniurb.it](mailto:achille.cappiello@uniurb.it)

## ORCID

Achille Cappiello: 0000-0002-6416-304X

Chris G. Gill: 0000-0001-7696-5894

‡ These authors contributed equally.

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## Standards and Solvents

All stock analyte solutions were prepared gravimetrically. Analyte sub-stocks and online additions of analytes were done volumetrically using a mechanical micropipette. Acetophenone (99%), biphenyl (99.5%), chlorobenzene (99.5%), and phenylacetylene (98%) were obtained from Sigma Aldrich (Oakville, ON, Canada). (*R*)- $\alpha$ -methyl benzylamine was obtained from Sigma Aldrich (Milan, Italy). Cyclohexane, NaCl, Na<sub>2</sub>SO<sub>4</sub> were obtained from Carlo Erba Reagents (Milan, Italy). Ethyl bromoacetate and triethylamine were purchased from VWR International (Milan, Italy). Acetonitrile, methanol, (HPLC grade) and ethyl acetate (99.9%) were obtained from VWR International (Edmonton, AB, Canada). Reagent alcohol (90% ethanol, 5% 2-propanol, 4.5% methanol, HPLC grade) and N,N-dimethylformamide (99.9%) were obtained from Fisher Scientific (Ottawa, ON, Canada). Reagent alcohol is referred to as ethanol for the purposes of this study. Dichloromethane ( $\geq 99.5\%$ ) was obtained from Sigma Aldrich. All analytical standards and reactants were ACS grade or better.

## Characterization of Alkyl Glycinate Standards

TLC (Cyclohexane:AcOEt, 60:40 v/v):  $R_f = 0.72$ ;

$[\alpha]_D = +33.56$  ( $c = 0.015$  M in CHCl<sub>3</sub>)

[Minor product Spectroscopic Characterization]:

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.44 – 7.20 (m, 5H), 4.20 (q,  $J = 6.9$  Hz, 1H), 4.13 (q,  $J = 7.1$  Hz, 4H), 3.57 (s, 4H), 1.35 (d,  $J = 6.7$  Hz, 3H), 1.24 (t,  $J = 7.1$  Hz, 6H); <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  171.528, 144.100, 128.460, 127.493, 127.284, 77.355, 77.038, 76.720, 60.957, 60.410, 52.400, 20.937, 14.189; MS ( $m/z$ ): 293

TLC (Cyclohexane:AcOEt, 60:40 v/v):  $R_f = 0.50$ ;

$[\alpha]_D = +70.62$  ( $c = 0.026$  M in CHCl<sub>3</sub>); Literature value for (S)- enantiomer =  $-64.4$  ( $c = 2.27$  g/mL in CHCl<sub>3</sub>)<sup>S-1</sup>;

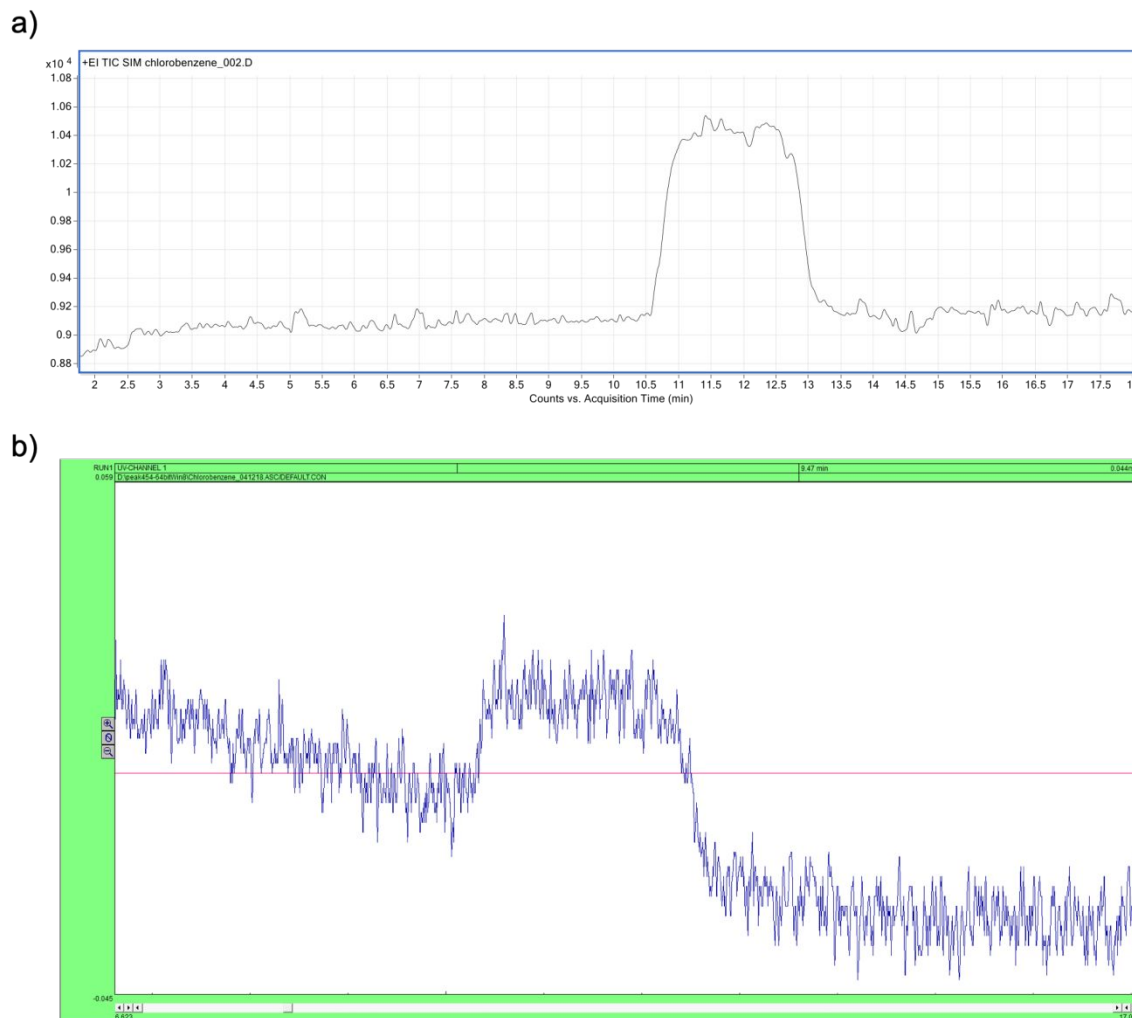
[Major product Spectroscopic Characterization]:

<sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  7.36 – 7.21 (m, 5H, Ar), 4.16 (q,  $J = 7.1$  Hz, 2H), 3.80 (q,  $J = 6.6$  Hz, 1H), 3.35 – 3.16 (m, 2H), 1.99 (s, 1H), 1.39 (d,  $J = 6.6$  Hz, 3H), 1.25 (t,  $J = 7.2$  Hz, 3H), <sup>13</sup>C

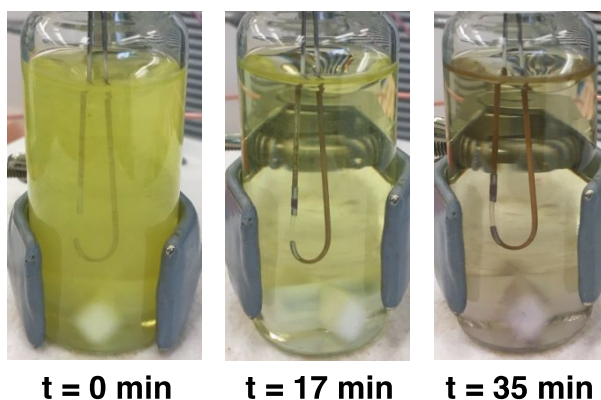
NMR (125 MHz,  $\text{CDCl}_3$ ):  $\delta$  172.548, 144.581, 128.496, 127.153, 126.742, 77.354, 77.039, 76.719, 60.687, 57.735, 48.863, 24.207, 14.18; MS ( $m/z$ ): 207

## References

- S-1. Porzi, G. & Sandri, S. Enantioselective synthesis of (R)- and (S)-  $\alpha$ -aminoacids using (6S)- and (6R)-6-methyl-morpholine-2,5-dione derivatives. *Tetrahedron: Asymmetry* **7**, 189-196 (1996).



**Figure S-1:** Chlorobenzene MS and UV-Vis recorded traces at a concentration of 25 mM. a) Data measured by CP-MIMS-LEI ( $m/z=112$ ); b) simultaneous UV-Vis spectrophotometry detection for 25 mM in methanol ( $\lambda=260$  nm)



**Figure S-2:** Images of PDMS membrane during the monitoring of the catalytic conversion of phenylacetylene to acetophenone

**Table S-1:** MS scan parameters

Analyte	MW / (g/mol)	Scan Type <sup>a</sup>	( <i>m/z</i> )	Collision Energy / (eV)
Acetophenone	120.15	SIM	105	-
Biphenyl	154.21	SIM	154	-
Chlorobenzene	112.56	SIM	112	-
Phenylacetylene	102.13	SIM	102	-
Ethyl bromoacetate	167.01	MRM (Quant)	121→93	10
		MRM (Qual)	138→120	5
$\alpha$ -Methylbenzylamine	121.18	MRM (Quant)	106→79	10
		MRM (Qual)	106→77	10
Mono-alkylated product	207.26	MRM (Quant)	192→91	10
		MRM (Qual)	192→118	10
Dialkylated product	293.34	MRM (Quant)	220→105	10
		MRM (Qual)	278→107	5

<sup>a</sup> Quant = quantitation transition, Qual = qualifying transition

**Table S-2:** Biphenyl calibrations and response times for 10-50 mM solute concentrations in various organic solvents

Solvent	Equation	R <sup>2</sup>	t <sub>10-90%</sub> (min)
Acetonitrile	y = 1.13x + 0.83	0.990	0.67
Dichloromethane	y = 5.39x – 4.36	0.999	0.41
N,N-Dimethylformamide	y = 0.50x + 1.70	0.983	0.63
Ethanol	y = 4.23x – 0.68	0.998	1.1
Methanol	y = 2.41x + 3.89	0.994	0.68

Triplicate measurements (intraday)

Risetimes calculated for 50 mM sample

**Table S-3:** Chlorobenzene calibrations and response times for 10-50 mM solute concentrations in various organic solvents

Solvent	Equation	R <sup>2</sup>	t <sub>10-90%</sub> (min)
Acetonitrile	y = 1.78x – 2.79	0.996	0.48
Dichloromethane	y = 5.24x + 2.83	1.000	0.33
N,N-Dimethylformamide	y = 1.62x – 2.27	0.996	0.43
Ethanol	y = 2.78x – 4.27	0.998	0.69
Methanol	y = 2.57x – 2.42	0.999	0.33

Triplicate measurements (intraday)

Risetimes calculated for 50 mM sample

**Table S-4:** Reactant and product calibrations and response times for oxidation reaction in methanol.

Analyte	Equation	R <sup>2</sup>	t <sub>10-90%</sub> (min)
Phenylacetylene	y = 16.8x – 29.7	0.999	0.35
Acetophenone	y = 5.33x – 1.79	1.000	0.40

Single Measurements in 95:4:1 methanol:de-ionized water:sulfuric acid v/v, 4 mM H<sub>2</sub>AuCl<sub>4</sub> with gentle heating (~50°C); 5-200 mM; Risetimes calculated for 90 mM sample

**Table S-5:** Reactant and product calibrations and response times for alkylation reaction in acetonitrile

Analyte	Equation	RSD (%) <sup>d</sup>	R <sup>2</sup>	t <sub>10-90%</sub> (min)
Ethyl bromoacetate <sup>a</sup>	y = 19.1x + 82.3	4	0.999	0.23
α-Methylbenzylamine <sup>a</sup>	y = 59.6x + 243	4	0.999	0.42
Mono alkylated product <sup>b</sup>	y = 16.1x + 68.3	-	0.999	0.60
Dialkylated product <sup>c</sup>	y = 4.85x + 1.36	-	1.000	1.2

<sup>a</sup> Triplicate measurements (interday); Linearity range: 1-500 mM; LOQ: 1 mM; Risetimes calculated for 250 mM sample

<sup>b</sup> Duplicate measurements (interday); Linearity range: 1-250 mM; LOQ: 1 mM; Risettime calculated for 250 mM sample

<sup>c</sup> Single measurements; Linearity range: 10-75 mM; LOQ: 10 mM; Risettime calculated for 75 mM sample

<sup>d</sup> Reagents RSD (%) was calculated for 250 mM sample. No available statistical data for mono and dialkylated products.